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EXAMINER	
PORTNER, VIRGINIA ALLEN	
ART UNIT	**PAPER NUMBER**
1645	12

DATE MAILED: 11/20/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application N .	Applicant(s)	
	09/928,457	NASSIF ET AL.	
	Examiner	Art Unit	
	Ginny Portner	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *14 August 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *65-105* is/are pending in the application.

4a) Of the above claim(s) *65-68,71-88 and 91-105* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *69,70,89 and 90* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *65-105* are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *1* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Claims 65-105 are pending.

Election/Restriction

1. Applicant's election with traverse of Group I, SEQ ID NO 95, in Region 4, in Paper No.11 is acknowledged. The traversal is on the ground(s) that the examiner has not shown undue burden, and examination of the entire application cannot constitute a serious burden. These arguments have been fully considered but are not found to be persuasive for the reasons below.

First, the classification system has no statutory recognition whether inventions are independent and distinct. For example, each class and subclass is comprised of numerous completely independent and distinct inventions.

Second, MPEP 803 states that restriction is proper between patentably distinct inventions where the inventions are (1)independent or distinct as claimed and (2) a serious search and examination burden is placed on the examiner if restriction is not required.

The term "distinct" is defined to mean that two or more subjects as disclosed are related, for example, as product and method of use, but are capable of separate manufacture, use or sale as claimed, and are patentable over each other (see MPEP 802.1). In the instant situation, the inventions of Groups I and II are drawn to distinct inventions which are related as separate products capable of separate functions. Restrictions between the inventions is deemed to be proper for the reason previously set forth.

In regard to burden of search and examination, MPEP 803 states that a burden can be shown if the examiner shows either separate classification, different field of search or separate status in the art. DNA and peptides differ by structure, function and biological effect. In the instant case a burden has been established in showing that the inventions of Groups I and II are classified separately necessitating different searches of issued US Patents 536/23.7 and 530/350. However, classification of subject matter is merely one indication of the burdensome nature of

search. The literature search, particularly relevant in this art, is not co-extensive, because for example proteins and peptides are identified by different methods of characterization that differ from the methods of identifying a DNA molecule. Additionally, it is submitted that the inventions of Groups I, each encoding a different peptide, have acquired a separate status in the art. Clearly different searches and issues are involved in the examination of each Group. For these reasons the restriction requirement is deemed to be proper and is therefore made Final.

2. **Claims 69-70 and 89-90 are under consideration; all other claims stand withdrawn from consideration.**

Ochiai/Brouwer Rejoinder

The examiner has required restriction between product and process claims. Where applicant elects claims directed to the product, and a product claim is subsequently found allowable, withdrawn process claims that depend from or otherwise include all the limitations of the allowable product claim will be rejoined in accordance with the provisions of MPEP § 821.04. Process claims that depend from or otherwise include all the limitations of the patentable product will be entered as a matter of right if the amendment is presented prior to final rejection or allowance, whichever is earlier. Amendments submitted after final rejection are governed by 37 CFR 1.116; amendments submitted after allowance are governed by 37 CFR 1.312.

In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103, and 112. Until an elected product claim is found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowed product claim will not be rejoined. See "Guidance on

Treatment of Product and Process Claims in light of *In re Ochiai, In re Brouwer* and 35 U.S.C. § 103(b)," 1184 O.G. 86 (March 26, 1996). Additionally, in order to retain the right to rejoinder in accordance with the above policy, Applicant is advised that the process claims should be amended during prosecution either to maintain dependency on the product claims or to otherwise include the limitations of the product claims. Failure to do so may result in a loss of the right to rejoinder.

Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01. The requirement is still deemed proper and is therefore made FINAL.

Priority

3. Acknowledgment is made of applicant's claim for foreign priority under 35 U.S.C. 119 (a)-(d). The certified copy has been filed in parent Application No. PCT/FR97/01295, filed on July 11, 1997.

Information Disclosure Statement

4. The information disclosure statement filed August 14, 2001 has been considered.

Sequence Compliance

5. The instant Application is in sequence compliance.

Specification

Content of Specification

6. At page 18, line 18, the header Brief Description of the Several Views of the Drawing(s) should be inserted. See MPEP § 608.01(f). A reference to and brief description of the drawing(s) as set forth in 37 CFR 1.74.

7. The disclosure is objected to because of the following informalities: The abstract recites the term "pilline"; the English term is --pilin--. Appropriate correction is required.

Claim Rejections - 35 U.S.C. § 112

8. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claims 69,70, 89 and 90 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 69, 89 are directed to an isolated DNA which is Neisseria meningitidis (Nm) specific and hybridizes on a Southern blot to a DNA sequence of Region 4 of Nm, and to a DNA sequence of MS11 (a Neisseria gonahorrea strain, Ng), but does not hybridize on a Southern blot to a DNA sequence of Neisseria lactamica (Nl).

The invention is directed to isolated DNA from any source or strain that will hybridize to Nm or Ng and is not present in Nl. The genus of isolated DNA molecules that can hybridize to any Region 4, based upon any arbitrary designation of a Region 4 of a Nm chromosome is claimed. No specific structural characteristics of Region 4 are set froth in claims 69 or 89, nor do the DNA molecules encode a peptide, polypeptide or protein of any specific structure of biological function. In light of claims 69 and 89 not defining a reference point to which the claimed DNA must hybridize under the recited hybridization conditions, and hybridization permitting a degree of change or variance from the reference DNA sequence (Z2491 and MS11), what the genus of claimed isolated DNA molecules are structurally are have not been described. No necessary common attributes or features of the elements are required other than hybridization to an arbitrary region 4; the reference region has not been described to evidence any common attributes or elements, therefore the claimed DNA molecules that would hybridize thereto have not been

described. No asserted correspondence to any known protein or polypeptides have been set forth in the claims for the isolated DNAs to encode. The invention is defined by what the isolated DNA is not through the recitation of negative limitations relative to Nl and additional protein coding sequences that are already known; what the claimed genus of DNAs are, has not been positively set forth in the claims. No specific structures correlated with function have been claimed as critical or essential characteristics of the claimed DNAs. The claimed genus of isolated DNAs have not been so described in such a way was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, that Applicant had possession of the claimed invention.

Claim 70 and 90 define the claimed invention to be a DNA or complement thereof to be a DNA of region 4 that will hybridize to a partial open reading frame structure of SEQ ID NO 95. SEQ ID NO 95 is not a complete open reading frame, but a partial sequence of 286 nucleotides in length, as the first three nucleotides correspond to the codon for Asn, and not a start codon "Met". What the reading frame is for the protein that is associated with "colonization of the nasopharynx or invasion of the submucosal space or systemic dissemination (functional claim limitations set forth in independent claim 69)", has not been described. It is not clear what number of additional nucleotides would be needed to obtain an entire coding sequence for a Nm or Ng protein; the protein has no specific biological function, and DNA is only defined to be "within an islet involved in the colonization". Which of the 6 possible reading frames the DNA or the complement must be read in order to obtain a protein associated with colonization has not been described. The claimed DNA must hybridize to SEQ ID NO 95, but what the additional nucleotides or the sequence of the claimed DNA that differs from SEQ ID NO 95 and encodes a protein associated with colonization has not been described. A representative number of species for the claimed genus have not been described by a combination of identifying characteristics, such as structure, correlated with function. A partial open reading frame is not representative of the genus of cDNA molecules because no information regarding the coding capacity of any cDNA

molecule would be disclosed. Further, defining the claimed cDNA in functional terms does not suffice in the absence of a disclosure of structural features or elements of a cDNA that would encode a protein having a stated function. What the size of the DNA of region 4 which will hybridize to the partial sequence, SEQ ID No 95, in an islet that has not been described to encode a protein of any specific structure correlated with any specific biological function, such as an enzyme, has not been described. While SEQ ID NO 95 has clearly been described, the claimed isolated DNAs or complements thereof from any region 4, which will hybridize to SEQ ID NO 95, have not been described by any other characteristics other than hybridization under the recited assay conditions, and not to encode any of the already known/recited proteins set forth in claim 69. What the claimed genus of isolated DNAs or complements are, which may be of any size or sequence that is larger or differs at location within the reference sequence has not been described.

10. The following is a quotation of the second paragraph of 35 U.S.C. 112:The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

11. Claims 69-70 and 89-90 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 69-70, 89-90 are directed to an isolated DNA which is Neisseria meningitidis (Nm) specific and hybridizes on a Southern blot to a DNA sequence of Region 4 of Nm, and to a DNA sequence of MS11 (a Neisseria gonahorrea strain, Ng). How can the claimed DNA be specific for Nm, and also hybridize to Ng? The preamble defines the claimed DNA to specific to Nm, but the body of the claim goes on to define that the claimed DNA is not specific for Nm, but specific to Nm and Ng. The invention is not distinctly claimed.

Claim 69, recites the phrase "or the complement of said isolated DNA"; does this phrase refer to the claimed DNA or the DNA of Neisseria lactamica? The phrase clearly refers back to some prior portion of the claim, but which portion it modifies is unclear as more than one DNA molecule is recited in the claim. Would the complement of the claimed DNA be an antisense DNA, cDNA or mRNA? Is the claim intended to include mRNA (cDNA) within the scope of the claims? What is being claimed through the recitation of "or the complement"? Clarification is requested.

Claim 69, paragraph 2, recites the introductory phrase "any one of the" and recites various proteins. Does this phrase refer only to the proteins involved in the biosynthesis of the polysaccharide capsule ? Or does the phrase "any one of the" also refer to the additionally recited terms in this paragraph and include "IgA proteases, pilin, a protein which binds transferrin". The term "or" is only recited between the terms "transferrin", "lactoferrin" and "an opacity protein". Which terms the introductory phrase refers is unclear.

Claims 69-70, 89 are unclear because what the region 4 is. What components are used to produce region 4? Region 4 has not been distinctly claimed. Regions of a bacterial chromosome can be arbitrarily defined based upon size, locations of specific coding sequences, and restriction endonuclease digestions. The instant specification utilizes a plurality of endonucleases to define and produce various regions of the bacterial chromosomes analyzed in the instant specification. The chromosome of Neisseria meningitidis Z2491 has been shown to be susceptible to a number of restriction endonucleases (see 1995 Table 1, page 6392, Dempsy et al) which all have at least four regions. None of the claims define which Region 4 is present or not present within the scope of the claimed invention through the broad recitation of the term "Region 4" in the claims. While stain Z2491 defines a specific starting material, what coding sequences, genes, probes and primers may be present in Region 4, is not distinctly claimed, in light of how Region 4 is made, or what is present in Region 4 is not positively recited; only what is not claimed is positively recited.

Claim 70 broadens the scope of claim 69; claim 69 is directed to DNA that will hybridize to region 4, while claim 70 is directed to DNA or mRNA (the complement of DNA) of region 4 which will hybridize to a reference sequence. The scope of claim 70 is both broadening and limiting, wherein two different molecules are claimed in claim 70, while claim 69 does not encompass both of the species set forth in claim 70.

Claim Rejections - 35 U.S.C. § 102

12. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in-
(1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effect under this subsection of a national application published under section 122(b) only if the international application designating the United States was published under Article 21(2)(a) of such treaty in the English language; or

(2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that a patent shall not be deemed filed in the United States for the purposes of this subsection based on the filing of an international application filed under the treaty defined in section 351(a).

13. Claims 69 and 89 are rejected under 35 U.S.C. 102(b) as being anticipated by Dempsey et al (November 1995). Dempsey et al disclose the instantly claimed invention directed to an isolated DNA (see Fig. 2, page 6396, an example of region 4, defined to include argJ to about regF; and is referred to as "6" in the SgfI map) which is present in both Neisseria meningitidis(Nm) and Neisseria gonorrhea (Ng) (see Figure 3, argJ is present in both Nm and Ng), and hybridizes on a Southern blot to a DNA sequence of Region 4 of Nm strain Z2491. The DNA

was combined with TBE buffer, a carrier (see page 6391, col. 1, materials and methods, paragraphs 2-3). Inherently the reference anticipates the instantly claimed invention.

14. Claims 69 and 89 are rejected under 35 U.S.C. 102(b) as being anticipated by Wolff et al (FEMS Microbiology Letters, Jan. 1995). Please Note: the examiner is reading the negative claim limitations set forth in paragraph 2, to be directed to complete open reading frames as the claim recites the term "gene", and permits the application of fragment portions against the claims.

Wolf et al disclose the instantly claimed invention directed to an isolated DNA that is Nm and Ng specific and does not hybridize with Neisseria lactamica (see page 257, Table 1, Rmp (an outer membrane protein) nucleotide sequence, and Figure 1, RMP/PIII DNA slot blot results showing no hybridization with N.lactamica strain 1855. The DNA was in association with a carrier (see section 2.2). Inherently the reference anticipates the instantly claimed invention.

15. Claims 69 and 89 are rejected under 35 U.S.C. 102(b) as being anticipated by Martin et al (accession number M65216, created date May 2, 1992) as evidenced by Swiss-Prot Blast alignment for argJ of Nm and Ng.

Martin et al disclose the instantly claimed invention directed to an isolated DNA that is present in region 4 defined by coding sequences between argJ and regF, and will hybridize to both Nm and Ng. The coding sequence for argJ, a gene encoding for ornithine acetyltransferase is one embodiment disclosed in the in instant specification at page 44, paragraph 2 to be in Region 4.

The DNA of Martin et al is a nucleic acid molecule (EMBL accession number M65216) that encodes argJ of Ng. The encoded protein shares 370 of 406 amino acids, 91% sequence identity at the amino acid level, with 100% sequence identity over at least the first 79 amino acids,amino acids 91-115, 116-254, and shows very little variance from 100% from about amino acids 280-

406. The amino acid sequence is encoded by the DNA molecule of Martin et al and would hybridize to Nm, as well as Ng. An argJ gene is not known to exist in Nl, and would therefore be Nm and Ng specific. Inherently the isolated DNA of Martin et al anticipates the instantly claimed invention.

16. Claims 69 and 89 are rejected under 35 U.S.C. 102(b) as being anticipated by Gaher et al 1996).

Gaher et al disclose the instantly claimed invention directed to an isolated DNA that is present in a Region 4, that is present in Neisseria gonorrhaeae strain MS11, as well as in Neisseria meningitidis Z2491(see Gaher, Figure 5, narrative, Fragment "E", hsp60 which is present in B1940, FA1090, and MS11.

The claimed nucleic acid in Region 4, includes the coding sequence for hsp60, a gene encoding for a heat shock protein (hsp60) which is disclosed by Gaher et al. Hsp60 is shown by Gaher et al to be present in MS11 (Ng), B1940 (Nm), and FA1090 (Nm). The nucleic acid encoding hsp60 is therefore present in both Nm and Ng, and in one embodiment of region 4 as defined by the instant specification. Inherently the isolated DNA of Gaher et al anticipates the instantly claimed invention.

17. Claims 69 and 89 are rejected under 35 U.S.C. 102(b) as being anticipated by Dempsey et al, 1994) as evidenced by Dempsey et al (1995).

Dempsey et al disclose the instantly claimed invention directed to an isolated DNA that is present in a Region 4, that is present in Neisseria gonorrhaeae, as well as in Neisseria meningitidis Z2491. Dempsey et al (1995) provide evidence that the DNA sequences of FA1090 are also

present in Z2491;See Dempsey et al (1995), Figure 3, Figure 2 *sgf*I, piece 6, includes hsp63 (aka, hsp60)) and will hybridize to both Nm and Ng). Inherently the DNA of Dempsey et al (1994) anticipates the instantly claimed invention.

Conclusion

18. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

19. Aho etal (1987) is cited to show an isolated DNA that is present in Nm, Ng but not Nl (see Table 1, Pilin column).

20. Eadie et al (US Pat. 5,445,933) is cited to show an Nm, Ng specific DNA molecule, that does not hybridize to Nl (see col. 5, Example 5, lines 45-52, and Figure 1).

21. Serizawa et al (1987) is cited to show an E.coli homolog of Nm and Ng regF, the E.coli homolog encoding a stringent starvation protein which shares about 45% sequence identity at the amino acid level with Nm and Ng (see sequence alignments provided)

22. Welcher et al (1986) is cited to show a method of substractive enrichment for Neisseria gonorrhea, and show the presence and absence of the isolated DNA with Nm (see Figures 2 and 5); in one well no hybridization was shown for Nl (Figure 5, Frame A).

23.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ginny Portner whose telephone number is (703)308-7543. The examiner can normally be reached on Monday through Friday from 7:30 AM to 5:00 PM except for the first Friday of each two week period.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith, can be reached on (703) 308-3909. The official fax phone number for this group is (703) 872-9306.

The Group and/or Art Unit location of your application in the PTO will be Group Art Unit 1645. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to this Art Unit.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Vgp

November 12, 2003

MARK NAVARRO
PRIMARY EXAMINER